CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-311

CORRESPONDENCE

noted jgs 2/27/01

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Philip Erickson, R.Ph.
Director, Regulatory Affairs
Solid Oral Dosage Forms

Phone: (215) 591 3000
FAX: (215) 591 8600

February 20, 2001

Gary Buehler, Acting Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

MINOR AMENDMENT

N/AM

ORIG AMENDMENT

ANDA #75-311
FAMOTIDINE TABLETS USP, 20 mg and 40 mg
MINOR AMENDMENT - "90 DAY AMENDMENT"

Dear Mr. Buehler:

We submit herewith a minor amendment to the above-referenced abbreviated new drug application (ANDA) in response to your review letter dated January 31, 2001. Specifically, this review letter notified us of an additional 6-months exclusivity period awarded to Merck and Co., Inc. regarding U.S. patent #4283408. As a result, the final approval date for the above-referenced ANDA has been pushed back to April 15, 2001 pursuant to 21 U.S.C. 355(j)(5)(D). For ease of review, please find in **Attachment 1** a copy of the January 31, 2001 review letter.

Please find below all chemistry, manufacturing, and control documents which have been revised since they were last provided to the Agency in either our ANDA or other amendments to the ANDA.

Famotidine, Raw Material Procedures Manual (AM-RM0094), determination of Famocyanoamidine - limit changed from . See **Attachment 2**.

There have been no changes to either our container labeling or our package insert labeling since they were submitted in our August 8, 2000 Minor Amendment and our October 4, 2000 Addendum to Minor Amendment, respectively.

This amendment is submitted for your review and final approval of ANDA #75-311. Please note that we anticipate receipt of final approval of our ANDA upon the extended expiration of U.S. patent # 4283408 for the reference listed drug, PEPCID® Tablets (Famotidine), 20 mg and 40 mg, on April 15, 2001. If there are any questions, please do not hesitate to contact me at (215) 591-3141 or facsimile at (215) 591-8812.

Sincerely,

PE/asg
Enclosures

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
FEB 2 1 2001
OGD

2/20/01

APOTHECON®
A Bristol-Myers Squibb Company
P.O. Box 4500 Princeton, NJ 08543-4500
609-897-2461 FAX: 609-897-5515

Elaine B. Cembor
Associate Director
Medical & Regulatory Operations

NEW CORRESP
NC

October 22, 1999

Mr. Paras Patel
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

Re: Famotidine Injection
10mg/mL, 2 mL Vials (Unpreserved)
ANDA 75-708
Withdrawal of Method of Use Patent Statement

Dear Mr. Patel:

Please refer to our abbreviated new drug application dated September 27, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Famotidine Injection, 10 mg/mL, 2 mL vials, and the phone conversation between Paras Patel of the FDA and Elaine Cembor of Apothecon, Inc. on October 22, 1999 requesting a withdrawal of the Method of Use Patent Statement.

As per your request, we are respectfully withdrawing the Method of Use Patent statement due to the fact that it refers to the process patent.

I apologize for any confusion this may have caused. I trust we have answered all concerns to the satisfaction of the Agency. Should you have any further concerns, please contact me by telephone at 609-897-2461 or by fax at 609-897-5515.

Sincerely,

EBCembor

Elaine B. Cembor
Associate Director
Regulatory Operations
777 Scudders Mill Rd.
Plainsboro, N. J. 08536

APOTHECON
A Bristol-Myers Squibb Company
P.O. Box 4500 Princeton, NJ 08543-4500
609-897-2461 FAX: 609-897-5515

Elaine B. Cembor
Associate Director
Medical & Regulatory Operations

NEW CORRESP

NC

October 13, 1999

Mr. Paras Patel
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

Re: Famotidine Injection
10mg/mL, 2 mL Vials (Unpreserved)

Dear Mr. Patel:

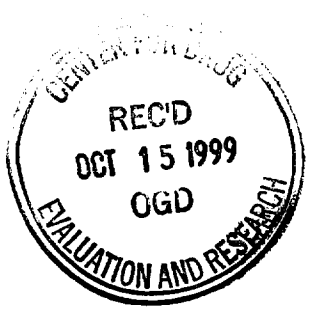
Please refer to our abbreviated new drug application dated September 27, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Famotidine Injection, 10 mg/mL, 2 mL vials, and the phone message from Paras Patel on October 13, 1999 requesting a revised 356h form with either Rx or OTC marked off.

Attached are two copies of the 356h form. One is for your review files and the other for your archived files. I apologize that the Rx status of the product was inadvertently left off the original form.

I trust we have answered all concerns to the satisfaction of the Agency. Should you have any further concerns, please contact me by telephone at 609-897-2461 or by fax at 609-897-5515.

Sincerely,

Elaine B. Cembor
Associate Director
Regulatory Operations
777 Scudders Mill Rd.
Plainsboro, N. J. 08536



ANDA 75-311

APR 16 2001

TEVA Pharmaceuticals USA
Attention: Philip Erickson
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454-1090

Dear Sir:

This is in reference to your abbreviated new drug application dated December 29, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Famotidine Tablets USP, 20 mg and 40 mg.

Reference is also made to your amendments dated February 20, and March 28, 2001.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Famotidine Tablets USP, 20 mg and 40 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Pepcid® Tablets, 20 mg and 40 mg, respectively, of Merck Research Laboratories). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Gary Buehler 4/16/01
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Philip Erickson, R.Ph.
Director, Regulatory Affairs
Solid Oral Dosage Forms

Phone: (215) 591 3000
FAX: (215) 591 8600

December 7, 2000

Gary Buehler, Acting Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

TELEPHONE AMENDMENT

NDA ORIG AMENDMENT

ANDA #75-311
FAMOTIDINE TABLETS USP, 20 mg and 40 mg
TELEPHONE AMENDMENT - RESPONSE TO DECEMBER 6, 2000 TELEPHONE REQUEST

Dear Mr. Buehler:

We submit herewith a telephone amendment to the above-referenced tentatively approved abbreviated new drug application in response to a telephone conversation between Dr. Karen Bernard of the Office of Generic Drugs and Philip Erickson, Director of Regulatory Affairs at TEVA Pharmaceuticals USA on December 6, 2000.

As requested we have revised the specification for
[redacted] substance specification summary is enclosed for your review.

In accord with the Agency's submission guideline dated November 8, 1991, we draw your attention to the essentially identical amendment to the following application:

ANDA #75-312 FAMOTIDINE TABLETS USP, 10 mg

This information is submitted for your continued review and approval of ANDA #75-311. If there are any further questions, please do not hesitate to contact me at (215) 591-3141 or via facsimile at (215) 591-8812

Sincerely,

Philip Erickson/RS

PE/brb
Enclosures

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
DEC 08 2000
OGD

noted 11/29/00 lms

TEVA

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Philip Erickson, R.Ph.
Director, Regulatory Affairs
Solid Oral Dosage Forms

ORIG AMENDMENT

N/Am

November 22, 2000

MINOR AMENDMENT

Gary Buehler, Acting Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ANDA #75-311
FAMOTIDINE TABLETS USP, 20 mg and 40 mg
MINOR AMENDMENT - RESPONSE TO NOVEMBER 6, 2000 REVIEW LETTER

Dear Mr. Buehler:

We submit herewith a minor amendment to the above-referenced abbreviated new drug application in accord with a November 6, 2000 review letter received from the Office of Generic Drugs. Specifically, the review letter requested additional information regarding acceptance criteria and method of quantitation for the process impurity in the active drug substance Famotidine USP. Please find a copy of the November 6, 2000 review letter in **Attachment 1**.

As a result of this request, TEVA has updated the procedures manual for Famotidine USP, AM- to include a test for determination of impurity with a specification of (which is the specification set by the supplier of this active ingredient). Please find a copy of this procedures manual in **Attachment 2**. In addition, please note that this manual was also updated to include a test for Melting Range determination (specification is between 160° - 164° C), which was added in accord with a July 21, 2000 review letter received by TEVA for Famotidine Chewable Tablets (ANDA # 75-821).

The Summary of Raw Material Specifications for Famotidine USP has been updated to reflect the specifications as stated above for determination of and Melting Range, and provided in **Attachment 3**.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
NOV 24 2000
OGD

20-622
N-1

This amendment is submitted for your review and final approval of ANDA #75-311. If there are any further questions, please do not hesitate to contact me at (215) 591-3141 or via facsimile at (215) 591-8812.

Sincerely,

PE/jbp
Enclosures

noted asg 8/10/00

Deborah A. Jaskot
Sr. Director, Regulatory Affairs

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
650 Cathill Road, Sellersville, PA 18960

Toll Free: (888) TEVA USA
Phone: (215) 256 8400
FAX: (215) 721 9669

Corresponding Address:
TEVA PHARMACEUTICALS USA
1510 Delp Drive, Kulpsville, PA 19443

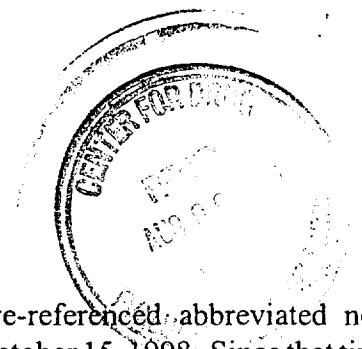
Toll Free: (888) TEVA USA
Phone: (215) 256 8400
FAX: (215) 256 7855

August 8, 2000

Gary Buehler, Acting Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

MINOR AMENDMENT

MINOR AMENDMENT



ANDA #75-311
FAMOTIDINE TABLETS USP, 20 mg and 40 mg
MINOR AMENDMENT - 90 DAY AMENDMENT

Dear Mr. Buehler:

We submit herewith a "90-Day" Amendment to the above-referenced abbreviated new drug application in accord with your tentative approval letter dated October 15, 1998. Since that time, there have been no CMC updates to this pending application. We have, however, modified our labeling to incorporate the recent changes to the insert labeling of the reference listed drug, PEPCID® Tablets (Famotidine), 20 mg and 40 mg. 12 copies of final print insert labeling is provided as **Attachment 1**. Also provided in this attachment is a comparison document detailing the revisions made between the insert labeling submitted in our June 19, 1998 Facsimile Amendment and that which is provided herein. Provided in **Attachment 2** are 12 copies of container labels which are identical to the draft labeling submitted for tentative approval.

This amendment is submitted for your review and final approval of ANDA #75-311. Please note that we anticipate receipt of final approval of our ANDA upon expiration of U.S. patent # 4283408 for the reference listed drug, PEPCID® Tablets (Famotidine), 20 mg and 40 mg, on October 15, 2000. If there are any questions, please do not hesitate to contact me at (215) 591-3000 ext. 5249 or facsimile at (215) 256-8105.

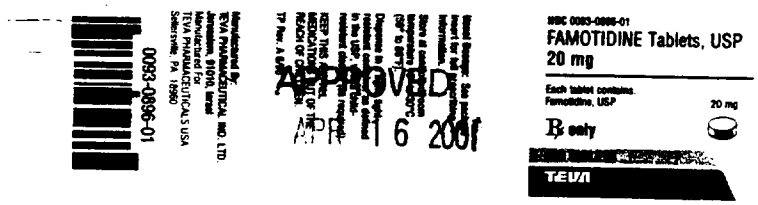
Sincerely,

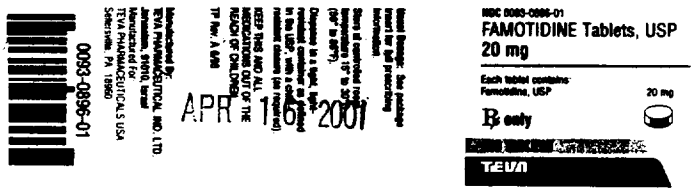
Deborah Jaskot

DAJ/asg
Enclosures

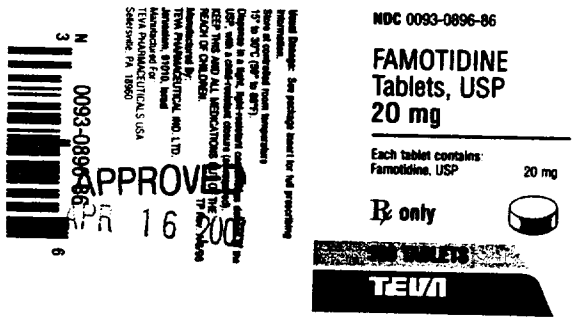
8-10

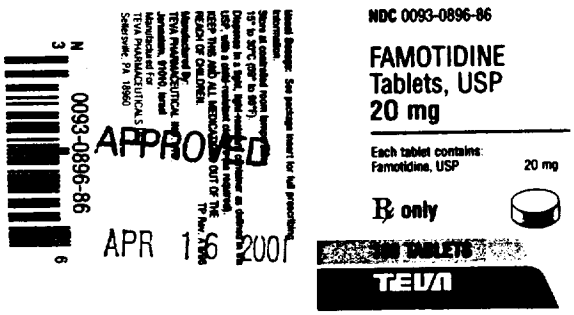
ANDA # 75-311
FAMOTIDINE TABLETS USP, 20 mg
CONTAINER LABELING (100 COUNT TABLETS)



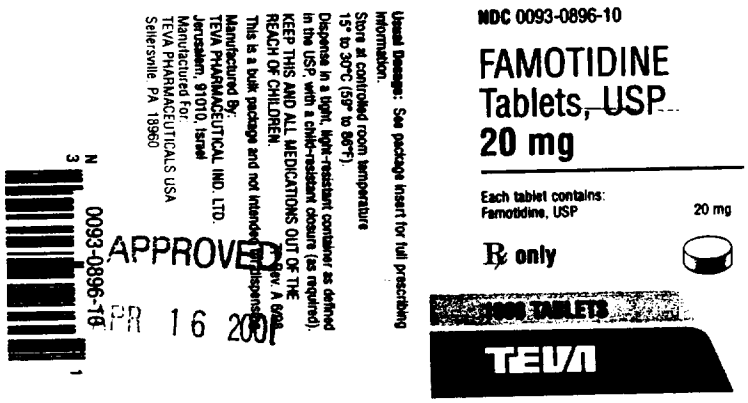


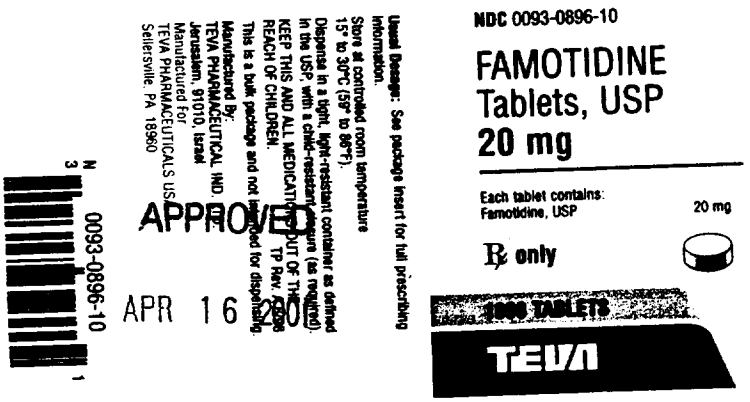
ANDA # 75-311
FAMOTIDINE TABLETS USP, 20 mg
CONTAINER LABELING (180 COUNT TABLETS)



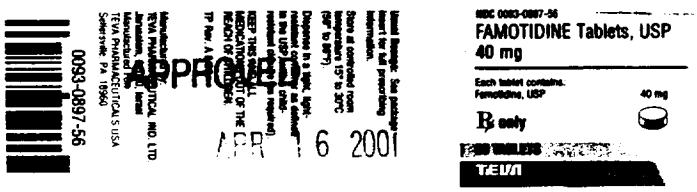


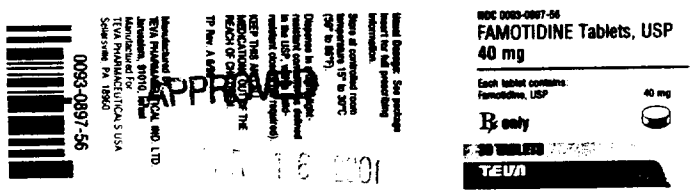
ANDA # 75-311
FAMOTIDINE TABLETS USP, 20 mg
CONTAINER LABELING (1000 COUNT TABLETS)





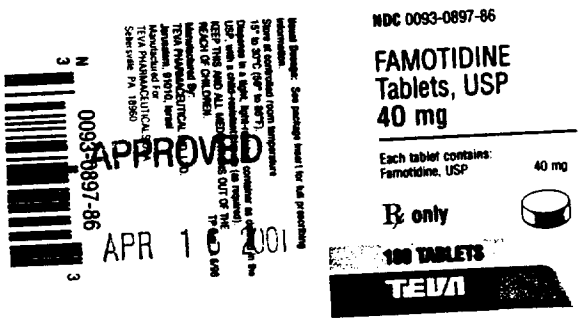
ANDA # 75-311
FAMOTIDINE TABLETS USP, 40 mg
CONTAINER LABELING (30 COUNT TABLETS)

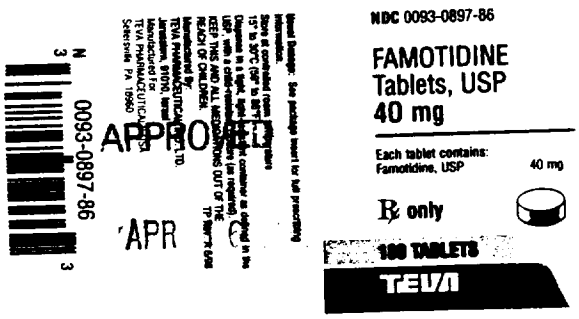




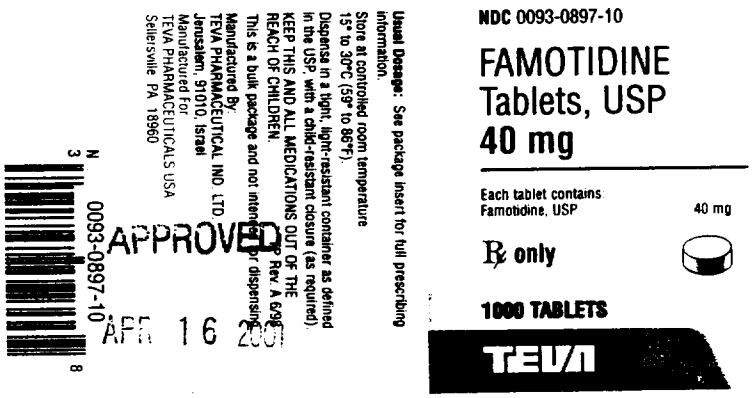
ANDA # 75-311
FAMOTIDINE TABLETS USP, 40 mg
CONTAINER LABELING (100 COUNT TABLETS)

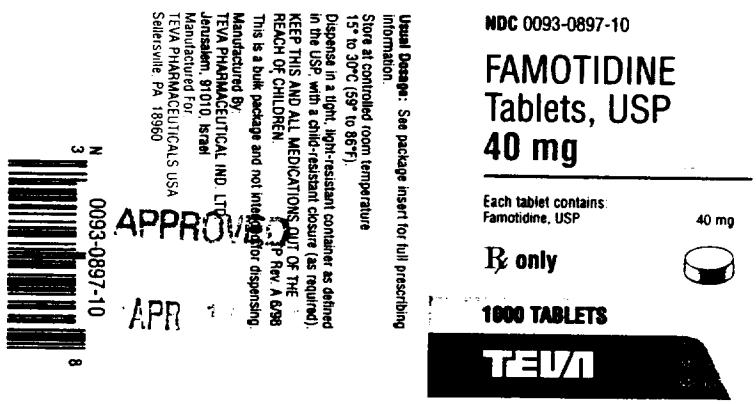
ANDA # 75-311
FAMOTIDINE TABLETS USP, 40 mg
CONTAINER LABELING (180 COUNT TABLETS)





ANDA # 75-311
FAMOTIDINE TABLETS USP, 40 mg
CONTAINER LABELING (1000 COUNT TABLETS)





OK to file
S. Middleton 3/6/98

Deborah A. Jaskot
Sr. Director, Regulatory Affairs

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
650 Cathill Road, Sellersville, PA 18960

Toll Free: (888) TEVA USA
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FAX : (215) 721 9669

Corresponding Address:
TEVA PHARMACEUTICALS USA
1510 Delp Drive, Kulpsville, PA 19443

Toll Free: (888) TEVA USA
Phone: (215) 256 8400
FAX: (215) 256 7855

December 29, 1997

Douglas Sporn, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIGINAL ABBREVIATED NEW DRUG APPLICATION
FAMOTIDINE TABLETS USP, 20 mg and 40 mg

Dear Mr. Sporn:

We submit herewith an abbreviated new drug application for the drug product Famotidine Tablets USP, 20 mg and 40 mg.

Enclosed are archival and review copies assembled in accord with Office of Generic Drugs April 1997 Guidance for Industry: Organization of an Abbreviated New Drug Application and an Abbreviated Antibiotic Application. These copies are presented in a total of 15 volumes; 7 for the archival copy and 8 for the review copy. The application contains a full report of two *in vivo* bioavailability studies. These studies compared **Famotidine Tablets USP, 40 mg** manufactured by TEVA Pharmaceutical Industries Ltd. to the reference listed drug, **Pepcid® Tablets (Famotidine), 40 mg** under fasting and post-prandial conditions. The application also contains a request for a waiver of evidence of *in vivo* bioavailability.

It was our intention to submit, in one application, Famotidine Tablets USP, 10 mg, 20 mg, and 40 mg. Upon further investigation and discussion with Lizzie Sanchez of the Division of Bioequivalence and Peter Rickman of your office, we were informed that two separate applications would be required, one for the 10 mg OTC and one for the 20 mg and 40 mg prescription strengths. As we received this information just prior to our intended submission, the headers of this application and some documents contained herein make reference to all dose strengths.

Please note that we have recently undergone a change in corporate name. As such, some documents may reference our previous name of LEMMON Company instead of the current name of TEVA Pharmaceuticals USA. No change in facilities, procedures, or commitments are made in conjunction with this change in name.

We look forward to your review and comment. Should you have any questions or need additional documentation, please do not hesitate to contact me at (215)-256-8400 ext. 5249.

Sincerely,

Deborah Jaskot

DAJ/ars
Enclosures

ANDA 75-311

OCT 15 1998

TEVA Pharmaceuticals, USA
Attention: Deborah A. Jaskot
1510 Delp Drive
Kulpsville, PA 19443

Dear Madam:

This is in reference to your abbreviated new drug application dated December 29, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Famotidine Tablets USP, 20 mg and 40 mg.

Reference is also made to your amendments dated February 5, and June 19, 1998.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted draft labeling. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product), and is therefore subject to change on the basis of new information that may come to our attention.

The listed reference drug product upon which you have based your application is subject to a period of patent protection and therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(4)(B)(ii) of the Act until the period has expired, i.e., October 15, 2000.

Please provide the Agency, at least 60, but not more than 90 days prior to October 15, 2000, an amendment to this application. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final printed labeling, chemistry, manufacturing, and controls data as appropriate. An

amendment should be submitted even if none of these changes were made. This submission should be designated as a MINOR AMENDMENT in your cover letter. In addition to, or instead of, the amendment requested above, the Agency may, at any time prior to the final date of approval, request that you submit an amendment containing the information described above.

Failure to submit such an amendment requested by the Agency will prompt a review of the application which may result in rescission of this tentative approval letter.

Any significant changes in the conditions outlines in this abbreviated application require Agency approval before the changes may be made effective.

Prior to issuance of a final approval letter by the Agency, your product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list, published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to October 15, 2000, you should amend your application accordingly.

At the time you submit any amendments, you should contact Kassandra Sherrod, Project Manager, at (301) 827-5849, for further instructions.

The introduction or delivery for introduction into interstate commerce of the drug before the effective approval date is prohibited under 21 U.S.C. 331(d).

Sincerely yours,

10/15/98

Roger L. Williams, M.D.
Deputy Center Director for
Pharmaceutical Science
Center for Drug Evaluation and Research

TEVA

Deborah A. Jaskot
Sr. Director, Regulatory Affairs

Corporate Headquarters:
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1510 Delp Drive, Kulpsville, PA 19443

Toll Free: (888) TEVA USA
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FAX: (215) 256 7855

June 19, 1998

NEW CORRESP
NC / hard copy

Douglas Sporn, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RECEIVED
JUN 22 1998
GENERIC DRUGS

FACSIMILE AMENDMENT

ANDA #75-311
FAMOTIDINE TABLETS USP, 20 mg and 40 mg
FACSIMILE AMENDMENT - RESPONSE TO REVIEW LETTER DATED MAY 20, 1998

Dear Mr. Sporn:

We herewith submit a facsimile amendment to the above referenced abbreviated new drug application in response to the review letter dated May 20, 1998. Our response is presented in the order in which the deficiencies were received.

A. Chemistry Deficiencies

1.

2.

USP procedure is the regulatory method and results obtained thereof will rule in the event of a dispute.

3.

B. In addition to the above deficiencies, we note and acknowledge the following:

1. We have revised FDA 356h form to list is provided in Attachment 2.

2. Samples of both the drug substance and the drug product will be available upon request from the FDA in accord with their instructions and 21 CFR 314.50 (e) (1).

3. You are correct that some of the certificates of analysis bottles as presented are technically bottle design conformance reports.

Labeling Deficiencies

1. Based on dispensing data, we do not view the package size of 100's as a unit-of-use package. As such, it is our intention to utilize a non-CRC (metal screw cap) as the closure for this container/closure system.

2. All labeling deficiencies have been addressed in the updated draft container and draft insert labeling as provided in Attachment 3.

   In addition to the above labeling deficiencies, we note and acknowledge that we will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. These final printed labels will differentiate the two different strengths from each other by using contrasting colors.

This information is submitted for your continued review and approval of ANDA 75-311. If you have any questions or comments regarding this submission, please do not hesitate to contact me at (215) 256-8400 ext. 5249 or via facsimile at (215) 256-8105.

Sincerely,

Deborah Jaskot/PE

DAJ/asg
Enclosures

ANDA 75-311

TEVA Pharmaceuticals USA
Attention: Deborah A. Jaskot
1510 Delp Drive
Kulpsville, PA 19443

FEB 13 1998

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Famotidine Tablets USP, 20 mg and 40 mg

DATE OF APPLICATION: December 29, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: January 2, 1998

We also acknowledge your correspondence dated February 5, 1998.

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Kassandra Sherrod
Project Manager
(301) 827-5849

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research